J.Cell.Mol.Med. Vol 6, No 4, 2002 pp. 451-452

Editorial Comment

Alive another day *

Neuroscience is facing the enormous demand to understand the basis of human aging and neurodegenerative disorders. With the increased age, the risk for most of the neurodegenerative disorders increases as well. How to analyse, how to prevent and how to manipulate those biologically inevitable events to prolong life is still an open question. The vast of our knowledge regarding human aging and neurodegenerative disorders comes from human post-mortem fixed material. Unfortunately, due to the species-specific differences, development of animal models cannot mirror a holistic picture of the human brain. Cell culturing of neuronal or non-neuronal human tissue does not fully answer the problems either. Thus it became imperative to conduct the experiments on human brain cells, which could be long-time maintained alive in cell culture and in the same time capable to keep functional properties as in intact brain. The dissociated cell cultures from adult human brain obtained after biopsies or autopsies could more or less increase availability of the cells but in a region-specific manner (peripheral nerve tissue mostly) or improving survival after manipulation with growth factors. Some recent findings indicate that isolation of progenitor cells from adult mammalian post-mortem brain could be possible. But successful maintenance of postmitotic adult human neuronal cells in culture was up to now almost an impossible task. *In a series of articles in the last two years the research group from Dutch Brain Bank in Amsterdam lead by Prof. Dick Swaab seems to turn a new page* in this respect. *They successfully cultured the slices of post-mortem human brain tissue* where the neuronal cells retained full morphological features and relative positions in the tissue towards other cellular elements within its natural environment, so called "trophic unit" (different glia cells, neuronal net, vessels etc.). The most intriguing was survival of the neurons up to almost 78 days of post-mortem time. Science fiction or not but this approach demands that certain preconditions need to be fulfilled such as: preparation of tissue within a 2–8 hours post-mortem delay, followed by carefully planed tissue dissection, maintenance and control procedure. The extensive studies were done on young and old brain tissue, different regions and different populations of cells. Surprisingly many neurons survive the hypoxic and ischemic conditions of death in face of post-mortem delay. Moreover it is very

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***** This editorial comment and the cover of this JCMM issue refers to **Verwer R.W.H. et al.,** "Tissue cultures from adult human postmortem subcortical brain areas", *J. Cell. Mol. Med.*, **6**:429-432, 2002.

straightforward that there is a selective regional, cellular and age-dependent vulnerability of the cells. For the first time it was possible to visualise the cells that maintain their activity even in the presence of pathological changes in the cytoplasm, findings that we could just guess in the histological "death" material. The metabolic activity, mitochondrial activity and even an interconnection pattern of the neurons can be easily studied. One can argue that foetal cell culture of non-human species can be easily used to study the neuronal aging as a function of the time – *in vitro* instead. It is plausible that post-mortem tissue culture of human neurons may display the aging features in continuation or even acceleration of aging processes starting earlier than patients death. Which one of these culture approaches mimics more "naturally" the aging processes is a matter to be proved in coming years. On the other hand, culturing human neuronal tissue with Alzheimer's, Parkinson, stroke and other neurodegenerative disease, has no alternative. While the state of the cells in animal brain tissue culture is almost identical, it is likely that the post-mortem human brain culture is characterized by a variability due to differences in diseases, co-morbidity factors, heredity and medication. Despite these difficulties which demand more careful analysis and more co-factors to be taken into account, the outcome of the studies on human post-mortem brain material can lead to more straightforward, "human specific" and more "natural" conclusions regarding aging and neurodegeneration. Moreover, human post-mortem brain cells that are affected or not by pathological changes can express the transgenes. Thus it can indicate that any disease-specific genetic or therapeutic intervention and manipulation could be possible. This methodological approach which is just born and as presented becomes a complementary to human *in vivo*-imaging and post-mortem histological methods. As a "newborn method" it needs the time to maturate and to be challenged to reach the decisive position in neuroscience research. We might be spectators or directly involved actors in this process but I am sure that scientists who want to study human aging and/or neurodegenerative diseases have to consider this method in a future. The main obstacle or limitation is or will be an accessibility of a well-characterised, short post-mortem human brain tissue. It will recurrently raise the issue of the importance to collect the human brain material as well as importance of wider public and scientific awareness. So dear brain bankers do not be surprised by the future requests, which may sound like ".....post-mortem human brain material but alive, please".

Nenad BOGDANOVIC M.D., Ph.D.

Karolinska Institute, NEUROTEC
Geriatric Department & Huddinge Brain Bank
KFC, NOVUM, plan4,
14186 Stockholm
Sweden